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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,186	04/16/2004	John Zeng Hui Zhang	57953/1221 (ZHA01-01)	8260

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Michael L. Goldman
NIXON PEABODY LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603

EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/825,186	ZHANG ET AL.	
	Examiner	Art Unit	
	KARLHEINZ R. SKOWRONEK	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-16,20-27 and 30-44* is/are pending in the application.

4a) Of the above claim(s) *39-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-16,20-27 and 30-39* is/are rejected.

7)☒ Claim(s) *1,16 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 30 December 2008 has been entered.

Claim Status

Claims 1-4, 7-16, 20-27, and 30-44 are pending.

Claims 5-6, 17-19 are cancelled.

Claims 39-44 are withdrawn as being directed to a non-elected invention the election made on 14 December 2006.

Claims 1-4, 7-16, 20-27, and 30-39 have been examined.

Claims 1-4, 7-16, 20-27, and 30-39 are rejected.

Claims 1, 16, and 27 are objected to.

Priority

This application was filed on 16 April 2004 and claims priority to prior US Provisional Application No. 60/463,753 which was filed on 17 April 2003.

Claim Objections

Claims 1, 16, and 27 are objected to because of the following informalities: Claims 1, 16, and 27 would be more precise if preposition "in" in the phrase "point in the" were exchanged with "of" in line 6 of claim 1, line 8 of claim 16 and, line 7 of claim 27; Claims 1, 16, and 27 would be more precise if the term "fragment" were "fragments" in line 6 of claim 1, in line 9 of claim 16, and in line 8 of claim 27. Appropriate correction is required.

Claim Rejections - 35 USC § 101

Response to Arguments

The rejection of claims 16 and 20-26 under 35 USC 101 as directed to non statutory subject matter is withdrawn in view of the amendments of the claims.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 and 7-15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-4 and 7-15 are directed to a process in which a molecular representation of a molecule is "decomposed" or split into at least two fragments, attaching at least a pair of atoms to the at least two fragments at the point of decomposition to generate molecular portions, forming at least a coupled cap by joining the pair of atoms, determining the interaction energies for the molecular portions with a second molecule and the coupled cap with the second molecule, calculating an interaction energy between the first and the second molecule

and displaying the calculated interaction energy between the first and second molecules. The following analysis is taken from the guidance provided in the MPEP at 2104.IV, "Determine Whether the Claimed Invention Complies with 35 USC101". The claims are directed to processes. Here the claims are directed to the abstract idea of calculating an interaction energy between a first and second molecule. The processes do not recite a physical transformation of matter from one state to another. Giving the claims the broadest reasonable interpretation, the claims read on mental steps. In *Comiskey* (*In re Comiskey*, 84 USPQ2d 1670) the court established that "the application of human intelligence to the solution of practical problems is not and of itself patentable" (at 1680). In *Comiskey*, the court stated explicitly "mental processes - or processes of human thinking - standing alone are not patentable even if they have a practical application" (at 1679). The court in *Comiskey* stated, "Following the lead of the Supreme Court, this court and our predecessor court have refused to find processes patentable when they merely claimed a mental process standing alone and untied to another category of statutory subject matter even when a practical application was claimed" (at 1680). The court's recent decision in *In re Bilski* confirmed, "a process is patent-eligible under 35 USC 101 if it is tied to a particular machine or apparatus or if it transforms a particular article into a different state or thing" (*In re Bilski*, 88 USPQ at 1391, 2008). In the instant claims, the process is not tied to a class of statutory invention.

Claims 1-4 and 7-15 recite providing an output or a response to a user. The output is insignificant post-solution activity and does not represent a significant tie to another category of invention. The court in *Comiskey*, stated "the court rejected the

notion that mere recitation of a practical application of an abstract idea makes it patentable, concluding that '[a] competent draftsman could attach some form of post-solution activity to almost any mathematical formula'" citing *Flook* (437 U.S. at 586, 590). The recent decision in *Bilski* confirmed the court's position regarding insignificant pre- or post-solution activity (i.e. insignificant extra-solution activity) as stated in *Comiskey* (see *In re Bilski*, 88 USPQ2d 1385 (Fed. Cir. 2008) at p. 13-96-1397). Applicant is encouraged to consider the recent BPAI informative decisions *Exparte Langemyr* (No. 2008-1495 (28 May 2008)) and *Exparte Biliski* (No. 2002-2257 (26 September 2006)) for further clarification of the above grounds of rejection.

Claim Rejections - 35 USC § 112

Response to Arguments

The rejection of claims 1-4, 7-16, 20-27, and 30-38 as introducing new matter under 35 USC 112, First Paragraph is withdrawn in view of the amendments to the claims.

The rejection of claims 1-4, 7-16, 20-27, and 30-38 as lacking written description under 35 USC 112, First Paragraph is withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1-4, 8-13, 16, 20-25, 27, and 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amovilli et al (Journal of Chemical Physics, Vol. 117, No.7, 15 August 2002), in view of Novosadov et al. (Journal of Structural Chemistry, Vol. 34, No.1, 27-32, 1993).

The claims are directed to a process in which a molecular representation of a molecule is "decomposed" or split into at least two fragments, attaching at least a pair of atoms to the at least two fragments at the point of decomposition to generate molecular portions, forming at least a coupled cap by joining the pair of atoms, determining the

interaction energies for the molecular portions with a second molecule and the coupled cap with the second molecule, calculating an interaction energy between the first and the second molecule and displaying the calculated interaction energy between the first and second molecules.

As defined at [0040] of the instant specification caps are atoms or radicals. The term conjugate cap is not explicitly defined in the specification to have a particular meaning. Based on the guidance provided in the specification, for example at [0038], a pair of caps contains 2 caps one cap for each fragment generated by decomposition of the first molecule. The specification, at [0038], further guides that one cap terminates the right side of the decomposition point and the other cap, its conjugate cap, terminates the left side of the decomposition point.

Amovilli et al shows a method of calculating intermolecular interaction energies of large molecules base on a fragmentation scheme. Amovilli et al. shows the method is based on an old suggestion which proposed that interaction energy for molecules could be approximated by the sum of atom-atom interactions by dividing a molecule into fragments and combining the interaction energies of the fragment (p.3003, col. 2). Amovilli et al shows the main advantage of this approach lies in the possibility of reducing the size of the calculations to fragments smaller than the molecules under study (p. 3003, col. 2). Amovilli et al shows the whole molecule is considered to be composed of a number of fragments which are the bricks to build the complete intermolecular potential energy (p. 3004, col. 1). Amovilli et al shows the choice of the fragment decomposition is guided by the requirement that the ground-state electron

density around the atoms in each fragment has to be as close as possible to that observed around the same atoms in the full molecule (p. 3004, col. 1). Amovilli et al shows a first molecule is decomposed into at least 2 fragments and the right and left sides of decomposition point are both capped with an atom, reading introducing a pair of conjugate caps (p. 3004, col. 1). In equation 1, Amovilli et al shows that first molecule is modeled as the sum of the capped fragments minus the contribution of the pair of caps. The contribution of the pair of caps is shown in equation 1 as, $-H_a - H_b$, which mathematically represents the coupling of the pair of caps. Amovilli et al shows the interaction energy is determined from the interaction energy of the molecular portions, A-H_a and B-H_b, with a second molecule X and the interaction energy of caps and the second molecule X (eqn. 3). Amovilli et al shows the determined interaction energies are used to calculate the interaction of the first molecule with the second molecule X (p. 3004, col. 2). Amovilli et al. shows that interaction energy determine by the method can be evaluated for all geometric conformations and can be used for simulations, suggesting the in silico limitations of claims 2-4 (p. 3012, col. 1). Regarding claim 8, Amovilli et al shows the energies of the molecular portions are summed to provide total interaction energy (eqn 3). Regarding claim 9, Amovilli et al shows in eqn. 3 that the contribution from the caps is summed and the total subtracted from the total interaction energy of the molecular portion. Regarding claim 11, Amovilli et al shows the first molecule is a polyatomic material, the biphenyl benzene 5CB (3010, col. 1). Regarding claim 13, Amovilli et al show the second molecule is an organic molecule, 5CB (p. 3006, col. 2).With respect to the limitations of a computer readable medium comprising

executable instructions and system of claims 16 and 27, respectively, Amovilli et al shows that a computer program was written to implement the method of calculating molecular interaction energy, suggesting a computer readable medium comprising executable instructions and system (p. 3010, col. 1).

Although Amovilli et al. does explicitly show the interaction energy is a quantum mechanical interaction energy, Amovilli et al does suggest it is possible to use ab initio quantum methods to evaluate the energies of the methods fragments.

Novsadov et al. shows that for large polyatomic molecules (large molecular systems) such as those important in biochemistry and pharmacology consist of 100-1000 or more atoms (p. 27). Novasadov et al. shows the quantum mechanical calculations of the fragments of the large molecular system can be used to construct a energetic description of total system (p. 27). Novosadov et al. shows the advantage of fragmenting large molecular system into small fragments for quantum mechanical energy calculations is that it economizes computer resources and enables one to handle a molecular system of any complexity (p. 27).

It would have been obvious to one of ordinary skill in the art to modify the method calculating molecular interaction energies of Amovilli et al to calculate quantum mechanical interaction energies because Novosadov et al shows the advantage of fragmenting large molecular system into small fragments for quantum mechanical energy calculations is that it economizes computer resources and enables one to handle a molecular system of any complexity.

Claim 7 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 above, and further in view of Shivarati et al (Computer, IEEE, Vol. 25, No.12, p.32-44, December 1992).

Claims 7 and 30 are directed to an embodiment in which the interaction energy calculations occur on a plurailty of computer systems.

Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 above shows a method of calculating molecular interaction energies.

Amovilli et al., in view of Novosadov et al. does not show the use of a pluraility of computers.

Shivarati et al shows that a plurality of computer can be interconnected as a distributed computing system. Shivarati et al shows that by performing a process called load balancing processes or tasks can be distributed to computers that are idle or lightly loaded (p. 33). Shivarati et al shows that load balancing has the advantage of improving system performance (p. 33). Shivarati et al shows the primary advantages of distributed computing systems are high performance, availability and extensibility at low cost (p. 33).

It would have been obvious to modify the method for calculating molecular interaction energies of Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 with the distributed computing of Shivarati et al. because Shivarati et al shows the primary advantages of distributed computing systems are high performance, availability and extensibility at low cost.

Claims 14 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 above, and further in view of Ewing et al. (Journal of Computer-aided Molecular Design, Vol. 15, p. 411-428, 2001).

Claim 14 and 37 are directed an embodiment in which the first molecule is a protein or peptide and the second molecule is a drug or water molecule.

Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 above shows a method of calculating molecular interaction energies.

Amovilli et al., in view of Novosadov et al. does not show the first molecule is a protein or peptide and the second molecule is a drug molecule.

Ewing shows that molecular interaction energies can be calculated between a first molecule that is protein or peptide and a second molecule that is a drug molecule (table 1). Ewing shows that water is also used as a second molecule (p. 416, col. 2). Ewing shows that the evaluation of molecular interactions between proteins and drugs is major component to structure based drug design (p. 411, col. 1).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the method for calculating molecular interaction energies of Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 with a first molecule that is a protein or peptide and a second molecule that is a drug of Ewing et al. because Ewing shows that the evaluation of molecular interactions between proteins and drugs is major component to structure based drug design.

Claims 15, 26, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 above, and further in view of Ante et al. (Journal of Physical Chemistry A, Vol. 103, No. 46, p. 9290-9295, 1999).

Claims 15, 26, and 38 are directed to an embodiment in which the caps are CH_3.

Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 above shows a method of calculating molecular interaction energies.

Amovilli et al., in view of Novosadov et al. does not show caps that are CH_3.

Ante et al shows the capping of molecular fragment with CH_3 (p. 9291, col. 1). Ante shows the benefit of using CH_3 as a cap is that it is advantageous to saturate each free valency of the QM region by a pseudoatom that occupies the same position as the neighboring MM atom in the bond being cut and that mimics its electronic influence as closely as possible (p. 9290, col. 2).

It would have been obvious to modify the method for calculating molecular interaction energies of Amovilli et al., in view of Novosadov et al. as applied to claims 1-4, 8-13, 16, 20-25, 27, and 31-36 with caps that are CH_3 as Ante et al. because Ante et al shows that it is advantageous to saturate each free valency of the QM region by a pseudoatom that occupies the same position as the neighboring MM atom in the bond being cut and that mimics its electronic influence as closely as possible.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571)272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KARLHEINZ R SKOWRONEK/
Examiner, Art Unit 1631

18 March 2009